Transdifferentiation and remodeling of post-embryonic C. elegans cells by a single transcription factor.

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Public Summary:
Fully developed cells in the body are generally considered irreversibly developmentally locked, i.e. incapable of being reprogrammed in vivo into entirely different cell types. We found that brief expression of a single transcription factor, a protein in the nucleus that controls gene expression, can convert the identity of fully differentiated, highly specialized mouth cell into an intestinal cells in living worms. Thus, cells that have stopped dividing, though terminally differentiated, can be remodeled adopt the characteristics of a new cell identity without removal of inhibitory factors. Our findings establish a simple model in the worm to investigate how cell context influences forced reprograming of mature cells, which might have relevance to treating human disease via a similar strategy.

Scientific Abstract:
Terminally differentiated post-mitotic cells are generally considered irreversibly developmentally locked, i.e. incapable of being reprogrammed in vivo into entirely different cell types. We found that brief expression of a single transcription factor, the ELT-7 GATA factor, can convert the identity of fully differentiated, highly specialized non-endodermal cells of the pharynx into fully differentiated intestinal cells in intact larvae and adult Caenorhabditis elegans. Stable expression of intestine-specific molecular markers parallels loss of markers for the original differentiated pharynx state; hence, there is no apparent requirement for a dedifferentiated intermediate during the transdifferentiation process. Based on high-resolution morphological characteristics, the transdifferentiated cells become remodeled to resemble typical intestinal cells at the level of both the cell surface and internal organelles. Thus, post-mitotic cells, though terminally differentiated, remain plastic to transdifferentiation across germ layer lineage boundaries and can be remodeled to adopt the characteristics of a new cell identity without removal of inhibitory factors. Our findings establish a simple model to investigate how cell context influences forced transdifferentiation of mature cells.